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Commentary

Cryo-EM Structure of Melbournevirus Reveals Flexible Strategies for Giant Virus Capsid Assembly

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Description

Giant viruses of the Nucleocytoplasmic Large DNA Virus (NCLDV) group possess complex capsid architectures that challenge conventional views of viral simplicity. Members of the Marseilleviridae family are particularly notable for their large icosahedral capsids and internal membrane extrusions at five-fold vertices. The recent cryo-Electron Microscopy (cryo-EM) structure of Melbournevirus at near-atomic resolution provides new insights into the organization and assembly of these viruses [1].

Using a block-based reconstruction approach [2] combined with symmetry expansion and defocus refinement, the Melbournevirus capsid was resolved to 4.9 Å globally and 4.42 Å locally. This study demonstrates that high-resolution structures of large viral particles (~ 250 nm diameter) can be achieved even with relatively small datasets when advanced computational corrections, such as Ewald sphere correction, are applied.

The Major Capsid Protein (MCP) adopts the conserved Double Jelly Roll (DJR) fold characteristic of NCLDVs, confirming a shared evolutionary origin among giant viruses. MCPs assemble into trimers stabilized by interactions involving extended loops and N-terminal domains. A distinctive feature of the Melbournevirus MCP is the formation of a "cup-like" structure at the top of each trimer, created by elongated surface loops. This structure accommodates an additional density attributed to a "cap" protein, likely corresponding to an abundant small viral protein identified in prior studies. Unlike the glycosylated caps of PBCV-1 or the extended domains of African Swine Fever Virus (ASFV), this cap represents a structurally distinct adaptation within Marseilleviridae.

At the five-fold vertices, a pentameric penton base protein with a single jelly roll fold forms the capsid vertex. A de novo polyalanine model reveals stabilization through both external loop interactions and internal terminal contacts. Beneath the penton, unresolved densities suggest the presence of additional components linking the capsid to the internal membrane extrusion, although these connections differ from those observed in other giant viruses.

A key finding of this study is the detailed visualization of the minor Capsid Protein (mCP) network. These proteins form a complex lattice beneath the MCP layer, including components termed Glue, Zipper, Cement, and Lattice protein components. Together, they stabilize interactions between capsomers and define the overall capsid geometry. Beneath this rigid layer, more flexible Scaffold and Support protein components connect the capsid shell to the internal membrane. These internal components likely contribute to structural adaptability and membrane organization.

Importantly, the study proposes that Scaffold protein components may substitute for the "tape measure proteins" described in other giant viruses, which are thought to regulate capsid size. In Melbournevirus, a distributed scaffold network appears to control capsid dimensions and assembly, suggesting an alternative strategy for achieving structural precision.

The arrangement of MCP trimers follows a conserved "golf club" motif, in which one trimer within each asymmetric unit is rotated by 60° [3]. This orientation facilitates proper alignment across symmetry boundaries and helps accommodate capsid curvature. In the absence of a clearly defined tape measure protein, this rotational pattern, together with the scaffold network, may play a central role in guiding capsid assembly.

Conclusion

In summary, the Melbournevirus structure highlights both conserved and flexible features of giant virus architecture. While the core MCP framework is preserved, variations in auxiliary proteins and assembly strategies demonstrate evolutionary adaptability. These findings provide a foundation for future studies aimed at fully resolving capsid composition and understanding the molecular mechanisms governing giant virus assembly.

References

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